

104 (New) A kit for treating cancer, comprising at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof, and a compound comprising:

- 5 a) a chelator;
- b) a targeting moiety;
- c) 0-1 linking groups between the targeting moiety and chelator;

wherein the targeting moiety is an indazole nonpeptide that  
10 binds to a receptor that is upregulated during angiogenesis.

Remarks

This is in response to the Restriction Requirement under 35 U.S.C. § 121, that was mailed  
15 April 4, 2001.

After the carrying out the amendments, claims 37-50, 58-104 will be pending.

The marked-up version of amended claims is found in Appendix I, attached to this Response, and titled "Marked-Up  
20 Version of Rewritten Claims". The amendments are shown by text stricken through to indicate deletions and underlined text to indicate insertions.

Claim 58 is amended to particularly point out and distinctly claim that which Applicants regard as their  
25 invention. In particular, claim 58 is amended to include the material of claim 2, which has been canceled. Support for the amendment is found throughout the application, for example on page 84, lines 15-21 and page 14, line 1 to page 31, line 4.  
30 Accordingly, no new matter is added.

Claim 59 is amended to particularly point out and distinctly claim that which Applicants regard as their invention. In particular, claim 59 is amended to include the material of claim 2, which has been canceled.  
35 Support for the amendment is found throughout the

application, for example on page 84, lines 23-33.

Accordingly, no new matter is added.

5        Claim 65 is amended to particularly point out and distinctly claim that which Applicants regard as their invention. In particular, claim 65 is amended to include the material of claim 11, which has been canceled. Support for the amendment is found throughout the application, for example on page 86, lines 28-35, and on page 12, lines 27-32.

10      Accordingly, no new matter is added.

      Claim 66 is amended to particularly point out and distinctly claim that which Applicants regard as their invention. In particular, claim 66 is amended to correct antecedent basis in the claim, in light of the  
15      amendment to claim 65. Support for the amendment is found throughout the application. Accordingly, no new matter is added.

      Claim 67 is amended to particularly point out and distinctly claim that which Applicants regard as their  
20      invention. In particular, claim 67 is amended to correct antecedent basis in the claim, in light of the amendment to claim 65. Support for the amendment is found throughout the application. Accordingly, no new matter is added.

25        Claim 68 is amended to particularly point out and distinctly claim that which Applicants regard as their invention. In particular, claim 68 is amended to include the material of claim 19, which has been  
30      canceled. Support for the amendment is found throughout the application, for example on page 13, lines 25-31, page 87 lines 36 to page 88 line 5 and on page 12, lines 27-32. Accordingly, no new matter is added.

New claim 76 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example in original claim 3, and 59. Accordingly, no new  
5 matter is added.

New claim 77 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 84, lines 15-21, and page 37, line 24, to page  
10 43, line 10. Accordingly, no new matter is added.

New claim 78 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 84, lines 15-21, and page 43, line 11 to page  
15 44, line 15. Accordingly, no new matter is added.

New claim 79 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 84, lines 15-21, and page 45, line 1, to page  
20 52, line 35. Accordingly, no new matter is added.

New claim 80 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 53, lines 6-8. Accordingly, no new matter is  
25 added.

New claim 81 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for on page 53, lines 10-11. Accordingly, no new matter is added.

New claim 82 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 53, lines 13-14. Accordingly, no new matter  
30 is added.

New claim 83 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, and page 57, lines 8-15.

5 Accordingly, no new matter is added.

New claim 84 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35 and page 58, lines 1-2.

10 Accordingly, no new matter is added.

New claim 85 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, page 57, lines 8-16, and page  
15 13, line 33, to page 31, line 4. Accordingly, no new matter is added.

New claim 86 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example  
20 on page 86, lines 28-35, page 57, lines 8-16, and page 31, line 5, to page 37, line 23. Accordingly, no new matter is added.

New claim 87 is added to claim that which Applicants regard as their invention. Support for this  
25 claim is found throughout the application, for example on page 86, lines 28-35, page 57, lines 8-16, and page 37, line 24, to page 43, line 10. Accordingly, no new matter is added.

New claim 88 is added to claim that which Applicants regard as their invention. Support for this  
30 claim is found throughout the application, for example on page 86, lines 28-35, page 57, lines 8-16, and page 43, line 12, to page 44, line 15. Accordingly, no new matter is added.

New claim 89 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, page 57, lines 8-16, and page 45, line 1, to page 52, line 35. Accordingly, no new matter is added.

New claim 90 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, and page 57, lines 8-16, and page 58, lines 3-8. Accordingly, no new matter is added.

New claim 91 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 58, lines 10-14. Accordingly, no new matter is added.

New claim 92 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, page 57, lines 8-16, and page 58, lines 15-16. Accordingly, no new matter is added.

New claim 93 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, to page 58, line 18, to page 59, line 5. Accordingly, no new matter is added.

New claim 94 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87, line 36, to page 88, line 5, page 57, lines 8-16, page 53, lines 16-24, and page 58, lines 1-2. Accordingly, no new matter is added.

New claim 95 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87, line 36, to page 88, line 5, page 57, lines 8-16, and  
5 page 13, line 33, to page 31, line 4. Accordingly, no new matter is added.

New claim 96 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87,  
10 line 36, to page 88, line 5, page 57, lines 8-16 and page 31, line 5, to page 37, line 22. Accordingly, no new matter is added.

New claim 97 is added to claim that which Applicants regard as their invention. Support for this claim is  
15 found throughout the application, for example on page 87, line 36, to page 88, line 5, page 57, lines 8-16, and page 37, line 24, to page 43, line 10. Accordingly, no new matter is added.

New claim 98 is added to claim that which Applicants regard as their invention. Support for this claim is  
20 found throughout the application, for example on page 87, line 36, to page 88, line 5, page 57, lines 8-16, and page 43, line 12, to page 44, line 15. Accordingly, no new matter is added.

New claim 99 is added to claim that which Applicants regard as their invention. Support for this claim is  
25 found throughout the application, for example on page 87 line 36, to page 88, line 5, page 57, lines 8-16, and page 45, line 1, to page 52, line 35. Accordingly, no  
30 new matter is added.

New claim 100 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87 line 36, to page 88, line 5, page 57, lines 8-16,

and page 58, lines 4-8. Accordingly, no new matter is added.

5 New claim 101 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87 line 36, to page 88, line 5, page 57, lines 8-16, and page 58, lines 10-14. Accordingly, no new matter is added.

10 New claim 102 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87 line 36, to page 88, line 5, page 57, lines 8-16, and page 58, lines 15-16. Accordingly, no new matter is added.

15 New claim 103 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87 line 36, to page 88, line 5, page 57, lines 8-16, and page 58, line 18, to page 59, line 5. Accordingly, 20 no new matter is added.

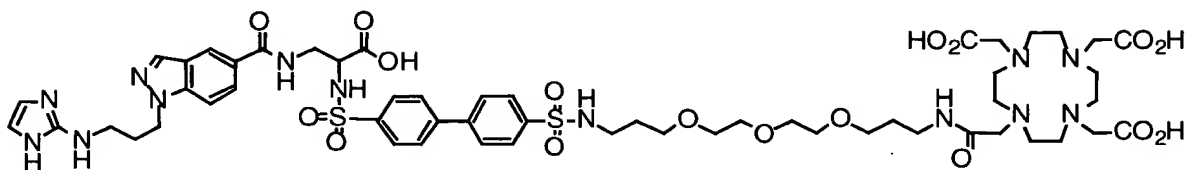
New claim 104 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 93, lines 26-30, page 13, lines 25-31 and page 113, 25 lines 10-18. Accordingly, no new matter is added.

#### Response to Restriction Requirement

In response to the outstanding restriction requirement, Applicants provisionally elect Group V with traverse. Applicants respectfully request 30 reconsideration and modification of the restriction to include the new claims 83 to 93 which are encompassed by elected Group V.

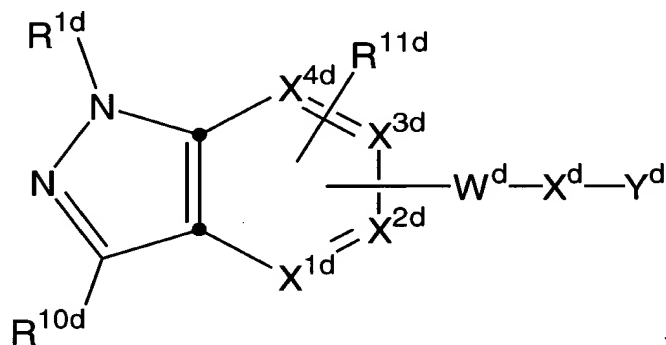
Also, as requested by the Examiner, Applicants elect Example 4, on page 142, as the species named: 35 3-((1-(3-(Imidazole-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)-2-(((4-(4-(((3-(2-(2-(3-(2-(1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl)-

acetyl amino) propoxy) ethoxy) ethoxy) propyl) amino) sulfonyl) -  
phenyl) phenyl) sulfonyl) amino) propanoic acid;  
having the formula:



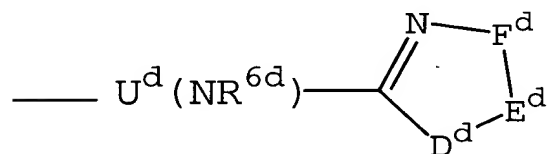
5

- Targeting Moiety: The targeting moiety is an indazole of formula:



wherein:

10  $\mathbb{R}^{1d}$  is



wherein:

$$D^d \text{ is } \mathbb{N}R^{2d} \text{ and } R^{2d} \text{ is } H;$$

$E^d - F^d$  is  $CR^{4d} = CR^{5d}$  and  $R^{4d}$  and  $R^{5d}$  are  $H$ ;

15  $U^d$  is  $(CH_2)_{n^d}$  and  $n^d$  is 3;

 $R^{6d}$  is  $H$ ; $R^{10d}$  is  $H$ ;

$X^{1d}, X^{2d}, X^{3d}, X^{4d}$  are  $C$ ;



$R^{11d}$  is H;

$W^d$  is  $C(=O)N(R^{13d}) - (C(R^{12d})_2)q^d$ ;

$R^{13d}$  is H;

$q^d$  is 0;

5  $X^d$  is  $CR^{12d}R^{14d}-CR^{12d}R^{15d}-$ ;

$R^{12d}$  is H;

$R^{14d}$  is H;

$R^{15d}$  is  $R^{16d}$ ;

$R^{16d}$  is  $N(R^{20d})SO_2R^{17d}$ ;

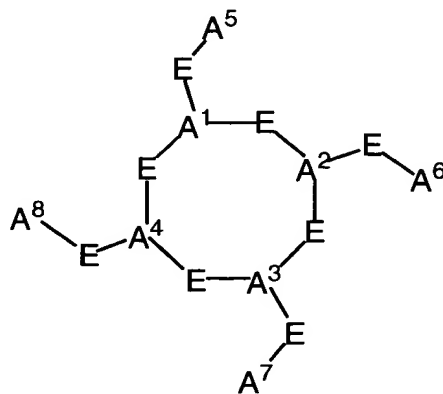
10  $R^{20d}$  is H;

$R^{17d}$  is a bond to Ln;

$Y^d$  is  $COR^{19d}$  and  $R^{19d}$  is OH; and

$d$  is 1.

- Method of Treatment: Applicants select a method of  
15 treating cancer.
- Chelator: The chelator is  $C_h$  given by the formula:



wherein:

- $A^1$ ,  $A^2$ ,  $A^3$ , and  $A^4$  are  $NR^{13}R^{14}$  wherein  $R^{13}$  and  $R^{14}$  are  
20 each an electron;

E (between A<sup>1</sup> and A<sup>2</sup>, A<sup>2</sup> and A<sup>3</sup>, A<sup>3</sup> and A<sup>4</sup>, and A<sup>4</sup> and A<sup>1</sup>) is CH<sub>2</sub>CH<sub>2</sub>;

A<sup>5</sup>, A<sup>6</sup>, and A<sup>7</sup> are OH;

A<sup>8</sup> is NR<sup>13</sup>R<sup>14</sup> wherein R<sup>13</sup> is H and R<sup>14</sup> is a bond to L<sub>n</sub>;

5 and

E (between A<sup>1</sup> and A<sup>5</sup>, A<sup>2</sup> and A<sup>6</sup>, A<sup>3</sup> and A<sup>7</sup>, and A<sup>4</sup> and A<sup>8</sup>) is CH<sub>2</sub>C(=O).

Applicants point out to the Examiner that this same compound was elected as the species in U.S. Patent application no. 09/281,207, now U.S. Patent No. 6,322,770.

Summary

Applicants submit that this application is in condition for allowance, a favorable action passing this case to issue is therefore respectfully requested. If a telephone interview would be of assistance in advancing prosecution of this application, Applicants' agent invites the Examiner to contact him at the number provided below.

20

Respectfully submitted,



25

Dated: February 7, 2002

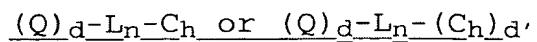
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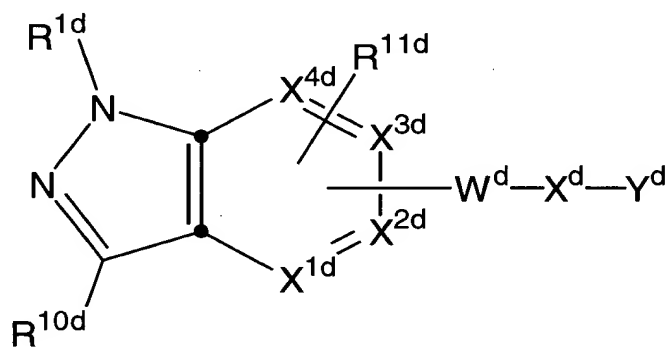
## Appendix I

Marked-Up Version of Rewritten Claims

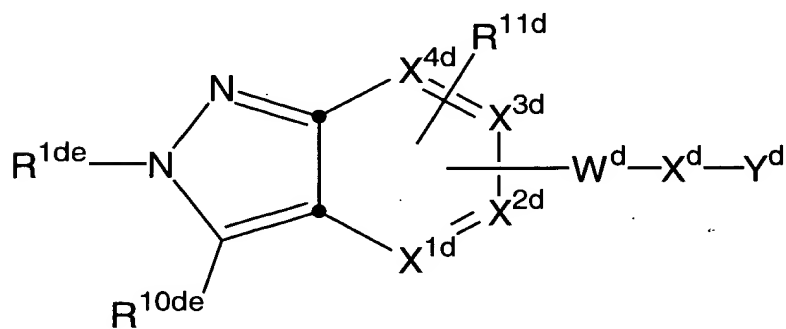
58. (Amended) A kit for treating cancer, ~~comprising a~~  
 5 ~~compound of~~ according to Claim 104 ~~Claim 1~~, wherein the  
compound is of the formula:



- 10 wherein, Q is independently a compound of Formula (Ia) or  
(Ib):



- 15 (Ia)



(Ib)

- 20 including stereoisomeric forms thereof, or mixtures of  
stereoisomeric forms thereof, or pharmaceutically  
acceptable salt or prodrug forms thereof wherein:

X<sup>1d</sup> is N, CH, C- W<sup>d</sup>- X<sup>d</sup>- Y<sup>d</sup>, or C-L<sub>n</sub>;

X<sup>2d</sup> is N, CH, or C- W<sup>d</sup>- X<sup>d</sup>- Y<sup>d</sup>;

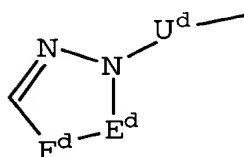
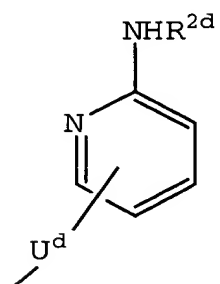
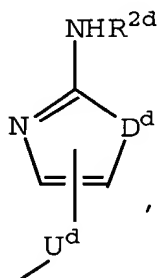
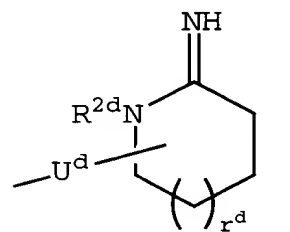
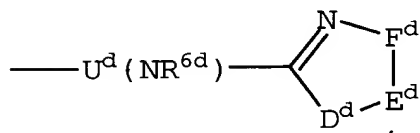
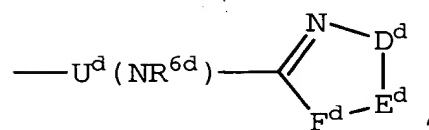
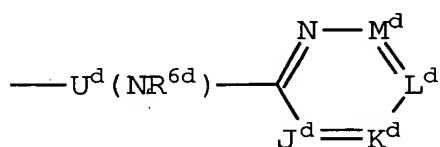
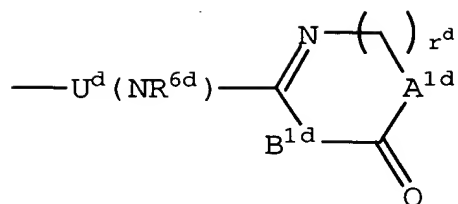
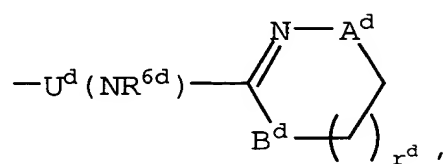
X<sup>3d</sup> is N, CR<sup>11d</sup>, or C- W<sup>d</sup>- X<sup>d</sup>- Y<sup>d</sup>;

5 X<sup>4d</sup> is N or CR<sup>11d</sup>;

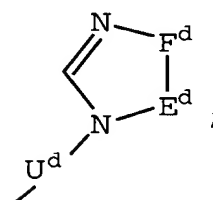
provided that when R<sup>1d</sup> is R<sup>1de</sup> then one of X<sup>1d</sup> and X<sup>2d</sup> is C- W<sup>d</sup>-  
X<sup>d</sup>- Y<sup>d</sup>, and when R<sup>10d</sup> is R<sup>1de</sup> then X<sup>3d</sup> is C- W<sup>d</sup>- X<sup>d</sup>- Y<sup>d</sup>;

10 R<sup>1d</sup> is selected from: R<sup>1de</sup>, C<sub>1</sub>-C<sub>6</sub> alkyl substituted with 0-1  
R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>6</sub> alkenyl substituted with 0-1 R<sup>15d</sup>  
or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>7</sub> cycloalkyl substituted with 0-1 R<sup>15d</sup> or  
0-1 R<sup>21d</sup>, C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl substituted with 0-1 R<sup>15d</sup>  
or 0-1 R<sup>21d</sup>, aryl substituted with 0-1 R<sup>15d</sup> or 0-2 R<sup>11d</sup> or  
15 0-1 R<sup>21d</sup>, and aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- substituted with 0-1 R<sup>15d</sup>  
or 0-2 R<sup>11d</sup> or 0-1 R<sup>21d</sup>;

R<sup>1de</sup> is selected from:



or



$A^d$  and  $B^d$  are independently  $-CH_2-$ ,  $-O-$ ,  $-N(R^{2d})-$ , or  $-C(=O)-$

A<sup>1d</sup> and B<sup>1d</sup> are independently -CH<sub>2</sub>- or -N(R<sup>3d</sup>)-;

D<sup>d</sup> is -N(R<sup>2d</sup>)-, -O-, -S-, -C(=O)- or -SO<sub>2</sub>-;

5

E<sup>d</sup>-F<sup>d</sup> is -C(R<sup>4d</sup>)=C(R<sup>5d</sup>)-, -N=C(R<sup>4d</sup>)-, -C(R<sup>4d</sup>)=N-, or  
-C(R<sup>4d</sup>)<sub>2</sub>C(R<sup>5d</sup>)<sub>2</sub>-;

J<sup>d</sup>, K<sup>d</sup>, L<sup>d</sup> and M<sup>d</sup> are independently selected from

10 -C(R<sup>4d</sup>)-, -C(R<sup>5d</sup>)- and -N-, provided that at least one of  
J<sup>d</sup>, K<sup>d</sup>, L<sup>d</sup> and M<sup>d</sup> is not -N-;

R<sup>2d</sup> is selected from: H, C<sub>1</sub>-C<sub>6</sub> alkyl, (C<sub>1</sub>-C<sub>6</sub> alkyl)carbonyl,  
15 (C<sub>1</sub>-C<sub>6</sub> alkoxy)carbonyl; (C<sub>1</sub>-C<sub>6</sub> alkyl)aminocarbonyl, C<sub>3</sub>-C<sub>6</sub>  
alkenyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl, aryl,  
heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)carbonyl, heteroarylcabonyl,  
aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, (C<sub>1</sub>-C<sub>6</sub> alkyl)carbonyl-, arylcarbonyl,  
C<sub>1</sub>-C<sub>6</sub> alkylsulfonyl, arylsulfonyl, aryl(C<sub>1</sub>-C<sub>6</sub>  
20 alkyl)sulfonyl, heteroarylsulfonyl, heteroaryl(C<sub>1</sub>-C<sub>6</sub>  
alkyl)sulfonyl, aryloxy carbonyl, and aryl(C<sub>1</sub>-C<sub>6</sub>  
alkoxy)carbonyl, wherein said aryl groups are substituted  
with 0-2 substituents selected from the group: C<sub>1</sub>-C<sub>4</sub>  
alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, halo, CF<sub>3</sub>, and nitro;

25 R<sup>3d</sup> is selected from: H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>4</sub>-C<sub>11</sub>  
cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, and  
heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

R<sup>4d</sup> and R<sup>5d</sup> are independently selected from: H, C<sub>1</sub>-C<sub>4</sub> alkoxy,

30 NR<sup>2d</sup>R<sup>3d</sup>, halogen, NO<sub>2</sub>, CN, CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> alkenyl,  
C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub>

alkyl)-, (C<sub>1</sub>-C<sub>6</sub> alkyl)carbonyl, (C<sub>1</sub>-C<sub>6</sub> alkoxy)carbonyl,  
and arylcarbonyl, or

alternatively, when substituents on adjacent atoms, R<sup>4d</sup> and R<sup>5d</sup>  
 5 can be taken together with the carbon atoms to which they  
are attached to form a 5-7 membered carbocyclic or 5-7  
membered heterocyclic aromatic or non-aromatic ring  
system, said carbocyclic or heterocyclic ring being  
optionally substituted with 0-2 groups selected from: C<sub>1</sub>-  
 10 C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, halo, cyano, amino, CF<sub>3</sub>, and NO<sub>2</sub>;

U<sup>d</sup> is selected from:

-(CH<sub>2</sub>)<sub>n<sup>d</sup></sub>-,  
-(CH<sub>2</sub>)<sub>n<sup>d</sup></sub>(CR<sup>7d</sup>=CR<sup>8d</sup>)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,  
 15 -(CH<sub>2</sub>)<sub>n<sup>d</sup></sub>(C≡C)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,  
-(CH<sub>2</sub>)<sub>t<sup>d</sup></sub>Q(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,  
-(CH<sub>2</sub>)<sub>n<sup>d</sup></sub>O(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,  
-(CH<sub>2</sub>)<sub>n<sup>d</sup></sub>N(R<sup>6d</sup>)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,  
-(CH<sub>2</sub>)<sub>n<sup>d</sup></sub>C(=O)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,  
 20 -(CH<sub>2</sub>)<sub>n<sup>d</sup></sub>(C=O)N(R<sup>6d</sup>)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-  
-(CH<sub>2</sub>)<sub>n<sup>d</sup></sub>N(R<sup>6d</sup>)(C=O)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-, and  
-(CH<sub>2</sub>)<sub>n<sup>d</sup></sub>S(O)<sub>p<sup>d</sup></sub>(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>;

wherein one or more of the methylene groups in U<sup>d</sup> is  
optionally substituted with R<sup>7d</sup>;

25 Q<sup>d</sup> is selected from 1,2-cycloalkylene, 1,2-phenylene, 1,3-  
phenylene, 1,4-phenylene, 2,3-pyridinylene, 3,4-  
pyridinylene, 2,4-pyridinylene, and 3,4-pyridazinylene;

30 R<sup>6d</sup> is selected from: H, C<sub>1</sub>-C<sub>4</sub> alkyl, and benzyl;

R<sup>7d</sup> and R<sup>8d</sup> are independently selected from: H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, and heteroaryl(C<sub>0</sub>-C<sub>6</sub> alkyl)-;

5

R<sup>10d</sup> is selected from: H, R<sup>1de</sup>, C<sub>1</sub>-C<sub>4</sub> alkoxy substituted with 0-1 R<sup>21d</sup>, N(R<sup>6d</sup>)<sub>2</sub>, halogen, NO<sub>2</sub>, CN, CF<sub>3</sub>, CO<sub>2</sub>R<sup>17d</sup>, C(=O)R<sup>17d</sup>, CONR<sup>17d</sup>R<sup>20d</sup>, -SO<sub>2</sub>R<sup>17d</sup>, -SO<sub>2</sub>NR<sup>17d</sup>R<sup>20d</sup>, C<sub>1</sub>-C<sub>6</sub> alkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>6</sub> alkenyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>7</sub> cycloalkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, aryl substituted with 0-1 R<sup>15d</sup> or 0-2 R<sup>11d</sup> or 0-1 R<sup>21d</sup>, and aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- substituted with 0-1 R<sup>15d</sup> or 0-2 R<sup>11d</sup> or 0-1 R<sup>21d</sup>;

10

15

R<sup>10de</sup> is selected from: H, C<sub>1</sub>-C<sub>4</sub> alkoxy substituted with 0-1 R<sup>21d</sup>, N(R<sup>6d</sup>)<sub>2</sub>, halogen, NO<sub>2</sub>, CN, CF<sub>3</sub>, CO<sub>2</sub>R<sup>17d</sup>, C(=O)R<sup>17d</sup>, CONR<sup>17d</sup>R<sup>20d</sup>, -SO<sub>2</sub>R<sup>17d</sup>, -SO<sub>2</sub>NR<sup>17d</sup>R<sup>20d</sup>, C<sub>1</sub>-C<sub>6</sub> alkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>6</sub> alkenyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>7</sub> cycloalkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, aryl substituted with 0-1 R<sup>15d</sup> or 0-2 R<sup>11d</sup> or 0-1 R<sup>21d</sup>, and aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- substituted with 0-1 R<sup>15d</sup> or 0-2 R<sup>11d</sup> or 0-1 R<sup>21d</sup>;

20

25

R<sup>11d</sup> is selected from H, halogen, CF<sub>3</sub>, CN, NO<sub>2</sub>, hydroxy, NR<sup>2d</sup>R<sup>3d</sup>, C<sub>1</sub>-C<sub>4</sub> alkyl substituted with 0-1 R<sup>21d</sup>, C<sub>1</sub>-C<sub>4</sub> alkoxy substituted with 0-1 R<sup>21d</sup>, aryl substituted with 0-1 R<sup>21d</sup>, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- substituted with 0-1 R<sup>21d</sup>,

30



(C<sub>1</sub>-C<sub>4</sub> alkoxy)carbonyl substituted with 0-1 R<sup>21d</sup>, (C<sub>1</sub>-C<sub>4</sub> alkyl)carbonyl substituted with 0-1 R<sup>21d</sup>, C<sub>1</sub>-C<sub>4</sub> alkylsulfonyl substituted with 0-1 R<sup>21d</sup>, and C<sub>1</sub>-C<sub>4</sub> alkylaminosulfonyl substituted with 0-1 R<sup>21d</sup>;

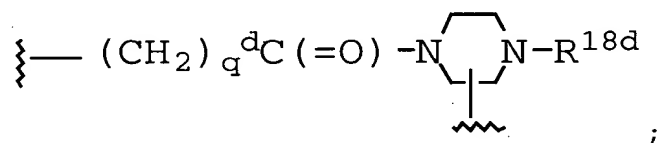
5

W<sup>d</sup> is selected from:

-(C(R<sup>12d</sup>)<sub>2</sub>)<sub>q</sub><sup>d</sup>C(=O)N(R<sup>13d</sup>)-, and

-C(=O)-N(R<sup>13d</sup>)-(C(R<sup>12d</sup>)<sub>2</sub>)<sub>q</sub><sup>d</sup>-;

10 X<sup>d</sup> is -C(R<sup>12d</sup>)(R<sup>14d</sup>)-C(R<sup>12d</sup>)(R<sup>15d</sup>)-; or  
alternatively, W<sup>d</sup> and X<sup>d</sup> can be taken together to be



15 R<sup>12d</sup> is selected from H, halogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>4</sub>-C<sub>10</sub> cycloalkylalkyl, (C<sub>1</sub>-C<sub>4</sub> alkyl)carbonyl, aryl, and aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

R<sup>13d</sup> is selected from H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkylmethyl,  
 20 and aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

R<sup>14d</sup> is selected from:

H, C<sub>1</sub>-C<sub>6</sub> alkylthio(C<sub>1</sub>-C<sub>6</sub> alkyl)-, aryl(C<sub>1</sub>-C<sub>10</sub> alkylthioalkyl)-, aryl(C<sub>1</sub>-C<sub>10</sub> alkoxyalkyl)-, C<sub>1</sub>-C<sub>10</sub> alkyl,  
 25 C<sub>1</sub>-C<sub>10</sub> alkoxyalkyl, C<sub>1</sub>-C<sub>6</sub> hydroxyalkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>2</sub>-C<sub>10</sub> alkynyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>3</sub>-C<sub>10</sub> cycloalkylalkyl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, aryl, heteroaryl, CO<sub>2</sub>R<sup>17d</sup>, C(=O)R<sup>17d</sup>, and CONR<sup>17d</sup>R<sup>20d</sup>, provided that any of the above alkyl, cycloalkyl, aryl or

heteroaryl groups may be unsubstituted or substituted independently with 0-1 R<sup>16d</sup> or 0-2 R<sup>11d</sup>;

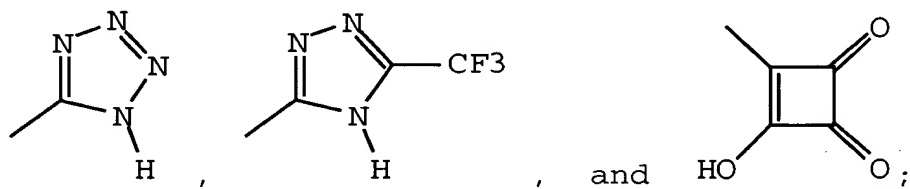
R<sup>15d</sup> is selected from:

- 5     H, R<sup>16d</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxyalkyl, C<sub>1</sub>-C<sub>10</sub> alkylaminoalkyl, C<sub>1</sub>-C<sub>10</sub> dialkylaminoalkyl, (C<sub>1</sub>-C<sub>10</sub> alkyl)carbonyl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)carbonyl, C<sub>1</sub>-C<sub>10</sub> alkenyl, C<sub>1</sub>-C<sub>10</sub> alkynyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>3</sub>-C<sub>10</sub> cycloalkylalkyl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, aryl,
- 10    heteroaryl, CO<sub>2</sub>R<sup>17d</sup>, C(=O)R<sup>17d</sup>, CONR<sup>17d</sup>R<sup>20d</sup>, SO<sub>2</sub>R<sup>17d</sup>, and SO<sub>2</sub>NR<sup>17d</sup>R<sup>20d</sup>, provided that any of the above alkyl, cycloalkyl, aryl or heteroaryl groups may be unsubstituted or substituted independently with 0-2 R<sup>11d</sup>;

- 15    Y<sup>d</sup> is selected from:

-COR<sup>19d</sup>, -SO<sub>3</sub>H, -PO<sub>3</sub>H, tetrazolyl, -CONHNHSO<sub>2</sub>CF<sub>3</sub>, -CONHSO<sub>2</sub>R<sup>17d</sup>, -CONHSO<sub>2</sub>NHR<sup>17d</sup>, -NHCOCF<sub>3</sub>, -NHCONHSO<sub>2</sub>R<sup>17d</sup>, -NHSO<sub>2</sub>R<sup>17d</sup>, -OPO<sub>3</sub>H<sub>2</sub>, -OSO<sub>3</sub>H, -PO<sub>3</sub>H<sub>2</sub>, -SO<sub>3</sub>H, -SO<sub>2</sub>NHCOR<sup>17d</sup>, -SO<sub>2</sub>NHCO<sub>2</sub>R<sup>17d</sup>,

20    \_\_\_\_\_



R<sup>16d</sup> is selected from:

- N(R<sup>20d</sup>)-C(=O)-O-R<sup>17d</sup>,
- 25    -N(R<sup>20d</sup>)-C(=O)-R<sup>17d</sup>,  
 -N(R<sup>20d</sup>)-C(=O)-NH-R<sup>17d</sup>,  
 -N(R<sup>20d</sup>)SO<sub>2</sub>-R<sup>17d</sup>, and  
 -N(R<sup>20d</sup>)SO<sub>2</sub>-NR<sup>20d</sup>R<sup>17d</sup>;

R<sup>17d</sup> is selected from:

5 C<sub>1</sub>-C<sub>10</sub> alkyl optionally substituted with a bond to L<sub>n</sub>, C<sub>3</sub>-  
C<sub>11</sub> cycloalkyl optionally substituted with a bond to L<sub>n</sub>,  
aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- optionally substituted with a bond to  
L<sub>n</sub>, (C<sub>1</sub>-C<sub>6</sub> alkyl)aryl optionally substituted with a bond  
to L<sub>n</sub>, heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- optionally substituted  
with a bond to L<sub>n</sub>, (C<sub>1</sub>-C<sub>6</sub> alkyl)heteroaryl optionally  
substituted with a bond to L<sub>n</sub>, biaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-  
optionally substituted with a bond to L<sub>n</sub>, heteroaryl  
10 optionally substituted with a bond to L<sub>n</sub>, aryl optionally  
substituted with a bond to L<sub>n</sub>, biaryl optionally  
substituted with a bond to L<sub>n</sub>, and a bond to L<sub>n</sub>, wherein  
said aryl, biaryl or heteroaryl groups are also  
optionally substituted with 0-3 substituents selected  
15 from the group consisting of: C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy,  
aryl, heteroaryl, halo, cyano, amino, CF<sub>3</sub>, and NO<sub>2</sub>;

R<sup>18d</sup> is selected from:

-H,  
20 -C(=O)-O-R<sup>17d</sup>,  
-C(=O)-R<sup>17d</sup>,  
-C(=O)-NH-R<sup>17d</sup>,  
-SO<sub>2</sub>-R<sup>17d</sup>, and  
-SO<sub>2</sub>-NR<sup>20d</sup>R<sup>17d</sup>;

25

R<sup>19d</sup> is selected from: hydroxy, C<sub>1</sub>-C<sub>10</sub> alkyloxy,

C<sub>3</sub>-C<sub>11</sub> cycloalkyloxy, aryloxy, aryl(C<sub>1</sub>-C<sub>6</sub> alkoxy)-, C<sub>3</sub>-C<sub>10</sub>  
alkylcarbonyloxyalkyloxy, C<sub>3</sub>-C<sub>10</sub>  
alkoxycarbonyloxyalkyloxy, C<sub>2</sub>-C<sub>10</sub> alkoxycarbonylalkyloxy,  
30 C<sub>5</sub>-C<sub>10</sub> cycloalkylcarbonyloxyalkyloxy,  
C<sub>5</sub>-C<sub>10</sub> cycloalkoxycarbonyloxyalkyloxy,  
C<sub>5</sub>-C<sub>10</sub> cycloalkoxycarbonylalkyloxy,

C<sub>7</sub>-C<sub>11</sub> aryloxy carbonylalkyloxy,  
C<sub>8</sub>-C<sub>12</sub> aryloxy carbonyloxyalkyloxy,  
C<sub>8</sub>-C<sub>12</sub> aryl carbonyloxyalkyloxy,  
C<sub>5</sub>-C<sub>10</sub> alkoxyalkyl carbonyloxyalkyloxy, C<sub>5</sub>-C<sub>10</sub> (5-alkyl-  
 5 1,3-dioxo-cyclopenten-2-one-yl)methyloxy, C<sub>10</sub>-C<sub>14</sub> (5-aryl-  
1,3-dioxo-cyclopenten-2-one-yl)methyloxy, and  
(R<sup>11d</sup>) (R<sup>12d</sup>)N-(C<sub>1</sub>-C<sub>10</sub> alkoxy)-;

10 R<sup>20d</sup> is selected from: H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>4</sub>-C<sub>11</sub>  
cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, and  
heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

R<sup>21d</sup> is selected from: COOH and NR<sup>6d</sup><sub>2</sub>;

m<sup>d</sup> is 0-4;

15 n<sup>d</sup> is 0-4;

t<sup>d</sup> is 0-4;

p<sup>d</sup> is 0-2;

q<sup>d</sup> is 0-2; and

r<sup>d</sup> is 0-2;

20

with the following provisos:

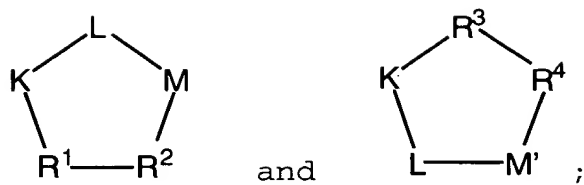
(1) t<sup>d</sup>, n<sup>d</sup>, m<sup>d</sup> and q<sup>d</sup> are chosen such that the number of atoms  
connecting R<sup>1d</sup> and Y<sup>d</sup> is in the range of 10-14; and

(2) n<sup>d</sup> and m<sup>d</sup> are chosen such that the value of n<sup>d</sup> plus m<sup>d</sup> is

25 greater than one unless U<sup>d</sup> is

-(CH<sub>2</sub>)<sub>t</sub><sup>d</sup> Q<sup>d</sup> (CH<sub>2</sub>)<sub>m</sub><sup>d</sup> -;

or Q is a peptide selected from the group:



R<sup>1</sup> is L-valine, D-valine or L-lysine optionally substituted on the ε amino group with a bond to L<sub>n</sub>;

5

R<sup>2</sup> is L-phenylalanine, D-phenylalanine, D-1-naphthylalanine, 2-aminothiazole-4-acetic acid or tyrosine, the tyrosine optionally substituted on the hydroxy group with a bond to L<sub>n</sub>;

10

R<sup>3</sup> is D-valine;

R<sup>4</sup> is D-tyrosine substituted on the hydroxy group with a bond to L<sub>n</sub>;

15

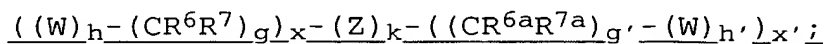
provided that one of R<sup>1</sup> and R<sup>2</sup> in each Q is substituted with a bond to L<sub>n</sub>, and further provided that when R<sup>2</sup> is 2-aminothiazole-4-acetic acid, K is N-methylarginine;

20 provided that at least one Q is a compound of Formula (Ia) or (Ib);

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

25 d' is 1-100;

L<sub>n</sub> is a linking group having the formula:



W is independently selected at each occurrence from the group:

5      O, S, NH, NHC(=O), C(=O)NH, NR<sup>8</sup>C(=O), C(=O)N R<sup>8</sup>, C(=O),  
C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO<sub>2</sub>, SO<sub>2</sub>NH,  
(OCH<sub>2</sub>CH<sub>2</sub>)<sub>s</sub>, (CH<sub>2</sub>CH<sub>2</sub>O)<sub>s</sub>', (OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>)<sub>s</sub>", (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>O)<sub>t</sub>, and  
(aa)<sub>t</sub>';

aa is independently at each occurrence an amino acid;

10      Z is selected from the group: aryl substituted with 0-3 R<sup>10</sup>,  
C<sub>3-10</sub> cycloalkyl substituted with 0-3 R<sup>10</sup>, and a 5-10  
membered heterocyclic ring system containing 1-4  
heteroatoms independently selected from N, S, and O and  
substituted with 0-3 R<sup>10</sup>;

15      R<sup>6</sup>, R<sup>6a</sup>, R<sup>7</sup>, R<sup>7a</sup>, and R<sup>8</sup> are independently selected at each  
occurrence from the group: H, =O, COOH, SO<sub>3</sub>H, PO<sub>3</sub>H, C<sub>1-C<sub>5</sub></sub>  
alkyl substituted with 0-3 R<sup>10</sup>, aryl substituted with 0-3  
R<sup>10</sup>, benzyl substituted with 0-3 R<sup>10</sup>, and C<sub>1-C<sub>5</sub></sub> alkoxy  
substituted with 0-3 R<sup>10</sup>, NHC(=O)R<sup>11</sup>, C(=O)NHR<sup>11</sup>,  
20      NHC(=O)NHR<sup>11</sup>, NHR<sup>11</sup>, R<sup>11</sup>, and a bond to C<sub>h</sub>;

25      R<sup>10</sup> is independently selected at each occurrence from the  
group: a bond to C<sub>h</sub>, COOR<sup>11</sup>, C(=O)NHR<sup>11</sup>, NHC(=O)R<sup>11</sup>, OH,  
NHR<sup>11</sup>, SO<sub>3</sub>H, PO<sub>3</sub>H, -OPO<sub>3</sub>H<sub>2</sub>, -OSO<sub>3</sub>H, aryl substituted with  
0-3 R<sup>11</sup>, C<sub>1-5</sub> alkyl substituted with 0-1 R<sup>12</sup>, C<sub>1-5</sub> alkoxy  
substituted with 0-1 R<sup>12</sup>, and a 5-10 membered  
heterocyclic ring system containing 1-4 heteroatoms  
independently selected from N, S, and O and substituted  
with 0-3 R<sup>11</sup>;

30      R<sup>11</sup> is independently selected at each occurrence from the  
group: H, alkyl substituted with 0-1 R<sup>12</sup>, aryl

substituted with 0-1  $R^{12}$ , a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1  $R^{12}$ ,  $C_{3-10}$  cycloalkyl substituted with 0-1  $R^{12}$ , polyalkylene glycol substituted with 0-1  $R^{12}$ , carbohydrate substituted with 0-1  $R^{12}$ , cyclodextrin substituted with 0-1  $R^{12}$ , amino acid substituted with 0-1  $R^{12}$ , polycarboxyalkyl substituted with 0-1  $R^{12}$ , polyazaalkyl substituted with 0-1  $R^{12}$ , and peptide substituted with 0-1  $R^{12}$ , wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to  $C_h$ ;

$R^{12}$  is a bond to  $C_h$ ;

15

$k$  is selected from 0, 1, and 2;

$h$  is selected from 0, 1, and 2;

$h'$  is selected from 0, 1, and 2;

$g$  is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

20 

$g'$  is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

$s$  is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

$s'$  is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

$s''$  is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

$t$  is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

25 

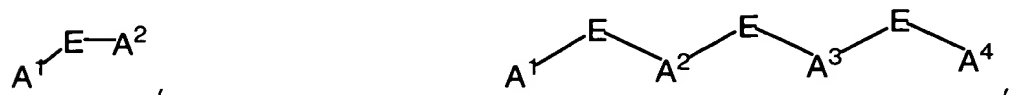
$t'$  is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

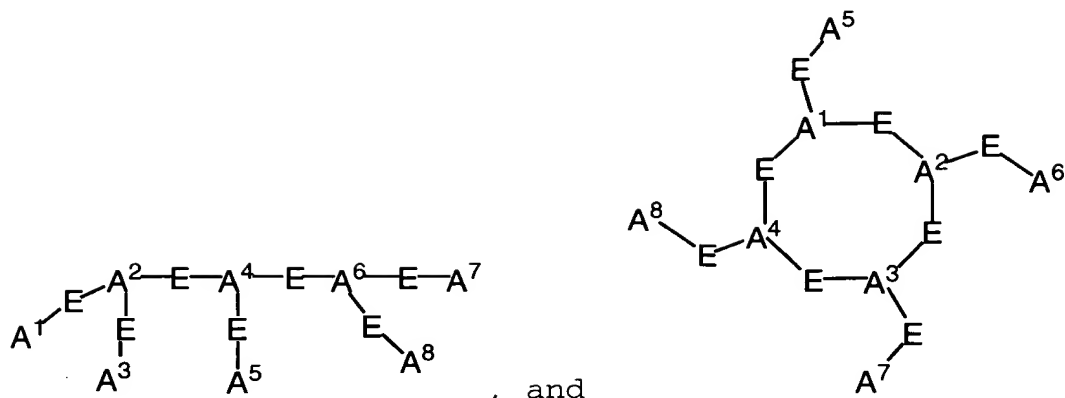
$x$  is selected from 0, 1, 2, 3, 4, and 5;

$x'$  is selected from 0, 1, 2, 3, 4, and 5;

30

$C_h$  is a metal bonding unit having a formula selected from the group:





$A^1$ ,  $A^2$ ,  $A^3$ ,  $A^4$ ,  $A^5$ ,  $A^6$ ,  $A^7$ , and  $A^8$  are independently selected at  
 5 each occurrence from the group:  $NR^{13}$ ,  $NR^{13}R^{14}$ , S, SH,  $S(Pg)$ , O, OH,  $PR^{13}$ ,  $PR^{13}R^{14}$ ,  $P(O)R^{15}R^{16}$ , and a bond to  $L_n$ ;

$E$  is a bond, CH, or a spacer group independently selected at  
 each occurrence from the group:  $C_1$ - $C_{10}$  alkyl substituted  
 10 with 0-3  $R^{17}$ , aryl substituted with 0-3  $R^{17}$ ,  $C_{3-10}$   
 cycloalkyl substituted with 0-3  $R^{17}$ , heterocyclo- $C_{1-10}$   
 alkyl substituted with 0-3  $R^{17}$ , wherein the heterocyclo  
 group is a 5-10 membered heterocyclic ring system  
 containing 1-4 heteroatoms independently selected from N,  
 15 S, and O,  $C_{6-10}$  aryl- $C_{1-10}$  alkyl substituted with 0-3  $R^{17}$ ,  
 $C_{1-10}$  alkyl- $C_{6-10}$  aryl- substituted with 0-3  $R^{17}$ , and a  
 5-10 membered heterocyclic ring system containing 1-4  
 heteroatoms independently selected from N, S, and O and  
 substituted with 0-3  $R^{17}$ ;

20  $R^{13}$  and  $R^{14}$  are each independently selected from the group: a  
 bond to  $L_n$ , hydrogen,  $C_1$ - $C_{10}$  alkyl substituted with 0-3  
 $R^{17}$ , aryl substituted with 0-3  $R^{17}$ ,  $C_{1-10}$  cycloalkyl  
 substituted with 0-3  $R^{17}$ , heterocyclo- $C_{1-10}$  alkyl  
 25 substituted with 0-3  $R^{17}$ , wherein the heterocyclo group



is a 5-10 membered heterocyclic ring system containing  
 1-4 heteroatoms independently selected from N, S, and O,  
C<sub>6-10</sub> aryl-C<sub>1-10</sub> alkyl substituted with 0-3 R<sup>17</sup>, C<sub>1-10</sub>  
alkyl-C<sub>6-10</sub> aryl- substituted with 0-3 R<sup>17</sup>, a 5-10  
 5 membered heterocyclic ring system containing 1-4  
 heteroatoms independently selected from N, S, and O and  
 substituted with 0-3 R<sup>17</sup>, and an electron, provided that  
 when one of R<sup>13</sup> or R<sup>14</sup> is an electron, then the other is  
 also an electron;

10

alternatively, R<sup>13</sup> and R<sup>14</sup> combine to form =C(R<sup>20</sup>)(R<sup>21</sup>);

15

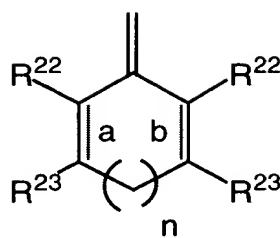
R<sup>15</sup> and R<sup>16</sup> are each independently selected from the group: a  
 bond to L<sub>n</sub>, -OH, C<sub>1-C10</sub> alkyl substituted with 0-3 R<sup>17</sup>,  
C<sub>1-C10</sub> alkyl substituted with 0-3 R<sup>17</sup>, aryl substituted  
 with 0-3 R<sup>17</sup>, C<sub>3-10</sub> cycloalkyl substituted with 0-3 R<sup>17</sup>,  
heterocyclo-C<sub>1-10</sub> alkyl substituted with 0-3 R<sup>17</sup>, wherein  
 the heterocyclo group is a 5-10 membered heterocyclic  
 ring system containing 1-4 heteroatoms independently  
 20 selected from N, S, and O, C<sub>6-10</sub> aryl-C<sub>1-10</sub> alkyl  
substituted with 0-3 R<sup>17</sup>, C<sub>1-10</sub> alkyl-C<sub>6-10</sub> aryl-  
substituted with 0-3 R<sup>17</sup>, and a 5-10 membered  
 heterocyclic ring system containing 1-4 heteroatoms  
 independently selected from N, S, and O and substituted  
 25 with 0-3 R<sup>17</sup>;

25

30

R<sup>17</sup> is independently selected at each occurrence from the  
 group: a bond to L<sub>n</sub>, =O, F, Cl, Br, I, -CF<sub>3</sub>, -CN,  
-CO<sub>2</sub>R<sup>18</sup>, -C(=O)R<sup>18</sup>, -C(=O)N(R<sup>18</sup>)<sub>2</sub>, -CHO, -CH<sub>2</sub>OR<sup>18</sup>,  
-OC(=O)R<sup>18</sup>, -OC(=O)OR<sup>18a</sup>, -OR<sup>18</sup>, -OC(=O)N(R<sup>18</sup>)<sub>2</sub>,  
-NR<sup>19</sup>C(=O)R<sup>18</sup>, -NR<sup>19</sup>C(=O)OR<sup>18a</sup>, -NR<sup>19</sup>C(=O)N(R<sup>18</sup>)<sub>2</sub>,

- NR<sup>19</sup>SO<sub>2</sub>N(R<sup>18</sup>)<sub>2</sub>, -NR<sup>19</sup>SO<sub>2</sub>R<sup>18a</sup>, -SO<sub>3</sub>H, -SO<sub>2</sub>R<sup>18a</sup>, -SR<sup>18</sup>,  
-S(=O)R<sup>18a</sup>, -SO<sub>2</sub>N(R<sup>18</sup>)<sub>2</sub>, -N(R<sup>18</sup>)<sub>2</sub>, -NHC(=S)NHR<sup>18</sup>, =NOR<sup>18</sup>,  
NO<sub>2</sub>, -C(=O)NHR<sup>18</sup>, -C(=O)NHN(R<sup>18</sup>)R<sup>18a</sup>, -OCH<sub>2</sub>CO<sub>2</sub>H,  
 5 2-(1-morpholino)ethoxy, C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>2</sub>-C<sub>4</sub> alkenyl, C<sub>3</sub>-C<sub>6</sub>  
cycloalkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylmethyl, C<sub>2</sub>-C<sub>6</sub> alkoxyalkyl,  
aryl substituted with 0-2 R<sup>18</sup>, and a 5-10 membered  
heterocyclic ring system containing 1-4 heteroatoms  
independently selected from N, S, and O;
- 10 R<sup>18</sup>, R<sup>18a</sup>, and R<sup>19</sup> are independently selected at each  
occurrence from the group: a bond to L<sub>n</sub>, H, C<sub>1</sub>-C<sub>6</sub> alkyl,  
phenyl, benzyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, halide, nitro, cyano, and  
trifluoromethyl;
- 15 Pg is a thiol protecting group;
- R<sup>20</sup> and R<sup>21</sup> are independently selected from the group: H,  
C<sub>1</sub>-C<sub>10</sub> alkyl, -CN, -CO<sub>2</sub>R<sup>25</sup>, -C(=O)R<sup>25</sup>, -C(=O)N(R<sup>25</sup>)<sub>2</sub>,  
C<sub>2</sub>-C<sub>10</sub> 1-alkene substituted with 0-3 R<sup>23</sup>, C<sub>2</sub>-C<sub>10</sub> 1-alkyne  
 20 substituted with 0-3 R<sup>23</sup>, aryl substituted with 0-3 R<sup>23</sup>,  
unsaturated 5-10 membered heterocyclic ring system  
containing 1-4 heteroatoms independently selected from N,  
S, and O and substituted with 0-3 R<sup>23</sup>, and unsaturated  
C<sub>3</sub>-C<sub>10</sub> carbocycle substituted with 0-3 R<sup>23</sup>;
- 25 alternatively, R<sup>20</sup> and R<sup>21</sup>, taken together with the divalent  
carbon radical to which they are attached form:



$R^{22}$  and  $R^{23}$  are independently selected from the group: H,  $R^{24}$ ,  
C<sub>1</sub>-C<sub>10</sub> alkyl substituted with 0-3  $R^{24}$ , C<sub>2</sub>-C<sub>10</sub> alkenyl  
 5 substituted with 0-3  $R^{24}$ , C<sub>2</sub>-C<sub>10</sub> alkynyl substituted with  
0-3  $R^{24}$ , aryl substituted with 0-3  $R^{24}$ , a 5-10 membered  
heterocyclic ring system containing 1-4 heteroatoms  
independently selected from N, S, and O and substituted  
with 0-3  $R^{24}$ , and C<sub>3</sub>-<sub>10</sub> carbocycle substituted with 0-3  
 10  $R^{24}$ ;

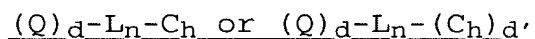
alternatively,  $R^{22}$ ,  $R^{23}$  taken together form a fused aromatic or  
a 5-10 membered heterocyclic ring system containing 1-4  
heteroatoms independently selected from N, S, and O;

15 **a** and **b** indicate the positions of optional double bonds and **n**  
is 0 or 1;

$R^{24}$  is independently selected at each occurrence from the  
 20 group: =O, F, Cl, Br, I, -CF<sub>3</sub>, -CN, -CO<sub>2</sub> $R^{25}$ , -C(=O) $R^{25}$ ,  
-C(=O)N( $R^{25}$ )<sub>2</sub>, -N( $R^{25}$ )<sub>3</sub><sup>+</sup>, -CH<sub>2</sub>OR<sup>25</sup>, -OC(=O) $R^{25}$ ,  
-OC(=O)OR<sup>25a</sup>, -OR<sup>25</sup>, -OC(=O)N( $R^{25}$ )<sub>2</sub>, -NR<sup>26</sup>C(=O) $R^{25}$ ,  
-NR<sup>26</sup>C(=O)OR<sup>25a</sup>, -NR<sup>26</sup>C(=O)N( $R^{25}$ )<sub>2</sub>, -NR<sup>26</sup>SO<sub>2</sub>N( $R^{25}$ )<sub>2</sub>,  
-NR<sup>26</sup>SO<sub>2</sub> $R^{25a}$ , -SO<sub>3</sub>H, -SO<sub>2</sub> $R^{25a}$ , -SR<sup>25</sup>, -S(=O) $R^{25a}$ ,  
 25 -SO<sub>2</sub>N( $R^{25}$ )<sub>2</sub>, -N( $R^{25}$ )<sub>2</sub>, =NOR<sup>25</sup>, -C(=O)NHOR<sup>25</sup>, -OCH<sub>2</sub>CO<sub>2</sub>H, and  
2-(1-morpholino)ethoxy; and,

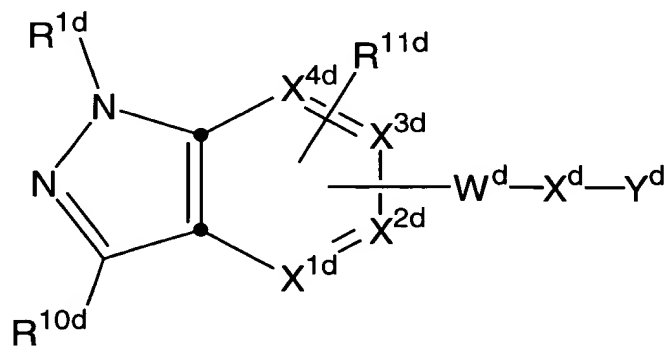
R<sup>25</sup>, R<sup>25a</sup>, and R<sup>26</sup> are each independently selected at each occurrence from the group: hydrogen and C<sub>1</sub>-C<sub>6</sub> alkyl.  
~~or a pharmaceutically acceptable salt thereof, and at least one agent selected from the group consisting of a~~  
 5 ~~chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.~~

59. (Amended) A kit according to claim 58 wherein said kit  
 10 comprises a plurality of separate containers, wherein at least one of said containers ~~contains a compound of Claim 1, or a pharmaceutically acceptable salt thereof, and at least another~~  
~~of said containers contains one or more agents selected from the group consisting of a chemotherapeutic agent and a~~  
 15 ~~radiosensitizer agent, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, and another of said containers contains a compound of formula:~~



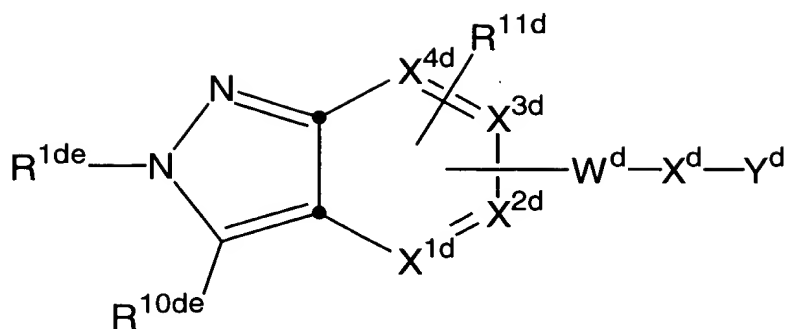
20

wherein, Q is independently a compound of Formula (Ia) or (Ib):



25

(Ia)



(Ib)

including stereoisomeric forms thereof, or mixtures of  
 5 stereoisomeric forms thereof, or pharmaceutically  
 acceptable salt or prodrug forms thereof wherein:

$X^{1d}$  is N, CH, C-  $W^d$ -  $X^d$ -  $Y^d$ , or C- $L_n$ ;

$X^{2d}$  is N, CH, or C-  $W^d$ -  $X^d$ -  $Y^d$ ;

10  $X^{3d}$  is N,  $CR^{11d}$ , or C-  $W^d$ -  $X^d$ -  $Y^d$ ;

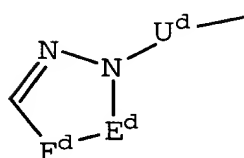
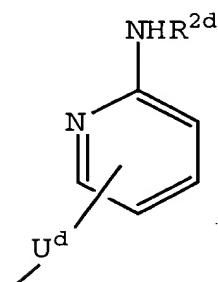
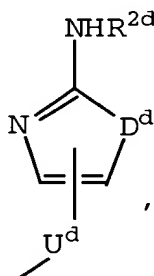
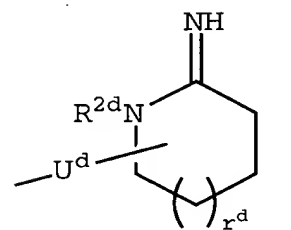
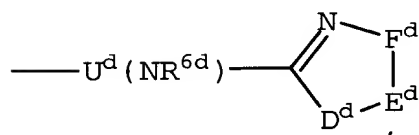
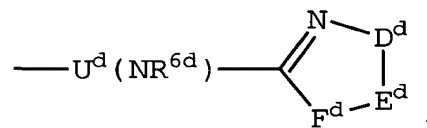
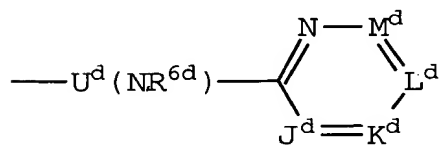
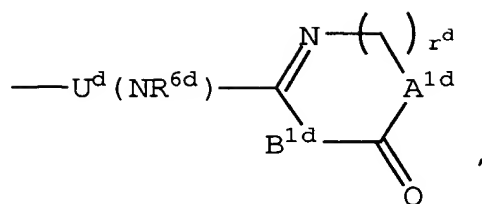
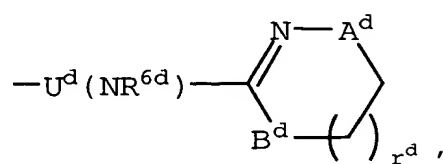
$X^{4d}$  is N or  $CR^{11d}$ ;

provided that when  $R^{1d}$  is  $R^{1de}$  then one of  $X^{1d}$  and  $X^{2d}$  is C-  $W^d$ -  
 $X^d$ -  $Y^d$ , and when  $R^{10d}$  is  $R^{1de}$  then  $X^{3d}$  is C-  $W^d$ -  $X^d$ -  $Y^d$ ;

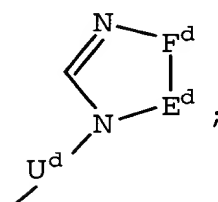
15

$R^{1d}$  is selected from:  $R^{1de}$ ,  $C_1$ - $C_6$  alkyl substituted with 0-1  
 $R^{15d}$  or 0-1  $R^{21d}$ ,  $C_3$ - $C_6$  alkenyl substituted with 0-1  $R^{15d}$   
 or 0-1  $R^{21d}$ ,  $C_3$ - $C_7$  cycloalkyl substituted with 0-1  $R^{15d}$  or  
 0-1  $R^{21d}$ ,  $C_4$ - $C_{11}$  cycloalkylalkyl substituted with 0-1  $R^{15d}$   
 20 or 0-1  $R^{21d}$ , aryl substituted with 0-1  $R^{15d}$  or 0-2  $R^{11d}$  or  
 0-1  $R^{21d}$ , and aryl( $C_1$ - $C_6$  alkyl)- substituted with 0-1  $R^{15d}$   
 or 0-2  $R^{11d}$  or 0-1  $R^{21d}$ ;

R<sup>1d</sup> is selected from:



or



5

A<sup>d</sup> and B<sup>d</sup> are independently -CH<sub>2</sub>-, -O-, -N(R<sup>2d</sup>)-, or -C(=O)-

A<sup>1d</sup> and B<sup>1d</sup> are independently -CH<sub>2</sub>- or -N(R<sup>3d</sup>)-;

D<sup>d</sup> is -N(R<sup>2d</sup>)-, -O-, -S-, -C(=O)- or -SO<sub>2</sub>-;

5

E<sup>d</sup>-F<sup>d</sup> is -C(R<sup>4d</sup>)=C(R<sup>5d</sup>)-, -N=C(R<sup>4d</sup>)-, -C(R<sup>4d</sup>)=N-, or  
-C(R<sup>4d</sup>)<sub>2</sub>C(R<sup>5d</sup>)<sub>2</sub>-;

J<sup>d</sup>, K<sup>d</sup>, L<sup>d</sup> and M<sup>d</sup> are independently selected from

10 -C(R<sup>4d</sup>)-, -C(R<sup>5d</sup>)- and -N-, provided that at least one of  
J<sup>d</sup>, K<sup>d</sup>, L<sup>d</sup> and M<sup>d</sup> is not -N-;

R<sup>2d</sup> is selected from: H, C<sub>1</sub>-C<sub>6</sub> alkyl, (C<sub>1</sub>-C<sub>6</sub> alkyl)carbonyl,  
(C<sub>1</sub>-C<sub>6</sub> alkoxy)carbonyl; (C<sub>1</sub>-C<sub>6</sub> alkyl)aminocarbonyl, C<sub>3</sub>-C<sub>6</sub>  
15 alkenyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl, aryl,  
heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)carbonyl, heteroarylcarbonyl,  
aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, (C<sub>1</sub>-C<sub>6</sub> alkyl)carbonyl-, arylcarbonyl,  
C<sub>1</sub>-C<sub>6</sub> alkylsulfonyl, arylsulfonyl, aryl(C<sub>1</sub>-C<sub>6</sub>  
alkyl)sulfonyl, heteroarylsulfonyl, heteroaryl(C<sub>1</sub>-C<sub>6</sub>  
20 alkyl)sulfonyl, aryloxycarbonyl, and aryl(C<sub>1</sub>-C<sub>6</sub>  
alkoxy)carbonyl, wherein said aryl groups are substituted  
with 0-2 substituents selected from the group: C<sub>1</sub>-C<sub>4</sub>  
alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, halo, CF<sub>3</sub>, and nitro;

25 R<sup>3d</sup> is selected from: H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>4</sub>-C<sub>11</sub>  
cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, and  
heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

R<sup>4d</sup> and R<sup>5d</sup> are independently selected from: H, C<sub>1</sub>-C<sub>4</sub> alkoxy,

30 NR<sup>2d</sup>R<sup>3d</sup>, halogen, NO<sub>2</sub>, CN, CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> alkenyl,  
C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub>

alkyl)-, (C<sub>1</sub>-C<sub>6</sub> alkyl)carbonyl, (C<sub>1</sub>-C<sub>6</sub> alkoxy)carbonyl,  
and arylcarbonyl, or

alternatively, when substituents on adjacent atoms, R<sup>4d</sup> and R<sup>5d</sup>  
 5 can be taken together with the carbon atoms to which they  
are attached to form a 5-7 membered carbocyclic or 5-7  
membered heterocyclic aromatic or non-aromatic ring  
system, said carbocyclic or heterocyclic ring being  
optionally substituted with 0-2 groups selected from: C<sub>1</sub>-  
 10 C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, halo, cyano, amino, CF<sub>3</sub>, and NO<sub>2</sub>;

U<sup>d</sup> is selected from:

-(CH<sub>2</sub>)<sub>n<sup>d</sup></sub>-,  
-(CH<sub>2</sub>)<sub>n<sup>d</sup></sub>(CR<sup>7d</sup>=CR<sup>8d</sup>)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,  
 15 -(CH<sub>2</sub>)<sub>n<sup>d</sup></sub>(C≡C)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,  
-(CH<sub>2</sub>)<sub>t<sup>d</sup></sub>Q(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,  
-(CH<sub>2</sub>)<sub>n<sup>d</sup></sub>O(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,  
-(CH<sub>2</sub>)<sub>n<sup>d</sup></sub>N(R<sup>6d</sup>)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,  
-(CH<sub>2</sub>)<sub>n<sup>d</sup></sub>C(=O)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,  
 20 -(CH<sub>2</sub>)<sub>n<sup>d</sup></sub>(C=O)N(R<sup>6d</sup>)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-  
-(CH<sub>2</sub>)<sub>n<sup>d</sup></sub>N(R<sup>6d</sup>)(C=O)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-, and  
-(CH<sub>2</sub>)<sub>n<sup>d</sup></sub>S(O)<sub>p<sup>d</sup></sub>(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>;

wherein one or more of the methylene groups in U<sup>d</sup> is  
optionally substituted with R<sup>7d</sup>;

25 Q<sup>d</sup> is selected from 1,2-cycloalkylene, 1,2-phenylene, 1,3-  
phenylene, 1,4-phenylene, 2,3-pyridinylene, 3,4-  
pyridinylene, 2,4-pyridinylene, and 3,4-pyridazinylene;

30 R<sup>6d</sup> is selected from: H, C<sub>1</sub>-C<sub>4</sub> alkyl, and benzyl;



R<sup>7d</sup> and R<sup>8d</sup> are independently selected from: H, C<sub>1</sub>-C<sub>6</sub> alkyl,  
C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub>  
alkyl)-,  
and heteroaryl(C<sub>0</sub>-C<sub>6</sub> alkyl)-;

5

R<sup>10d</sup> is selected from: H, R<sup>1de</sup>, C<sub>1</sub>-C<sub>4</sub> alkoxy substituted with  
0-1 R<sup>21d</sup>, N(R<sup>6d</sup>)<sub>2</sub>, halogen, NO<sub>2</sub>, CN, CF<sub>3</sub>, CO<sub>2</sub>R<sup>17d</sup>,  
C(=O)R<sup>17d</sup>, CONR<sup>17d</sup>R<sup>20d</sup>, -SO<sub>2</sub>R<sup>17d</sup>,  
-SO<sub>2</sub>NR<sup>17d</sup>R<sup>20d</sup>, C<sub>1</sub>-C<sub>6</sub> alkyl substituted with 0-1 R<sup>15d</sup> or 0-1  
R<sup>21d</sup>, C<sub>3</sub>-C<sub>6</sub> alkenyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>,  
C<sub>3</sub>-C<sub>7</sub> cycloalkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>,  
C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl substituted with 0-1 R<sup>15d</sup> or 0-1  
R<sup>21d</sup>, aryl substituted with 0-1 R<sup>15d</sup> or 0-2 R<sup>11d</sup> or 0-1  
R<sup>21d</sup>, and aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- substituted with 0-1 R<sup>15d</sup> or  
0-2 R<sup>11d</sup> or 0-1 R<sup>21d</sup>;

10

15

R<sup>10de</sup> is selected from: H, C<sub>1</sub>-C<sub>4</sub> alkoxy substituted with 0-1  
R<sup>21d</sup>, N(R<sup>6d</sup>)<sub>2</sub>, halogen, NO<sub>2</sub>, CN, CF<sub>3</sub>, CO<sub>2</sub>R<sup>17d</sup>, C(=O)R<sup>17d</sup>,  
CONR<sup>17d</sup>R<sup>20d</sup>, -SO<sub>2</sub>R<sup>17d</sup>, -SO<sub>2</sub>NR<sup>17d</sup>R<sup>20d</sup>, C<sub>1</sub>-C<sub>6</sub> alkyl  
substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>6</sub> alkenyl  
substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>7</sub> cycloalkyl  
substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>4</sub>-C<sub>11</sub>  
cycloalkylalkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>,  
aryl substituted with 0-1 R<sup>15d</sup> or 0-2 R<sup>11d</sup> or 0-1 R<sup>21d</sup>, and  
aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- substituted with 0-1 R<sup>15d</sup> or 0-2 R<sup>11d</sup> or  
0-1 R<sup>21d</sup>;

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25

R<sup>11d</sup> is selected from H, halogen, CF<sub>3</sub>, CN, NO<sub>2</sub>, hydroxy,  
NR<sup>2d</sup>R<sup>3d</sup>, C<sub>1</sub>-C<sub>4</sub> alkyl substituted with 0-1 R<sup>21d</sup>, C<sub>1</sub>-C<sub>4</sub>  
alkoxy substituted with 0-1 R<sup>21d</sup>, aryl substituted with  
0-1 R<sup>21d</sup>, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- substituted with 0-1 R<sup>21d</sup>,

30

(C<sub>1</sub>-C<sub>4</sub> alkoxy)carbonyl substituted with 0-1 R<sup>21d</sup>, (C<sub>1</sub>-C<sub>4</sub> alkyl)carbonyl substituted with 0-1 R<sup>21d</sup>, C<sub>1</sub>-C<sub>4</sub> alkylsulfonyl substituted with 0-1 R<sup>21d</sup>, and C<sub>1</sub>-C<sub>4</sub> alkylaminosulfonyl substituted with 0-1 R<sup>21d</sup>;

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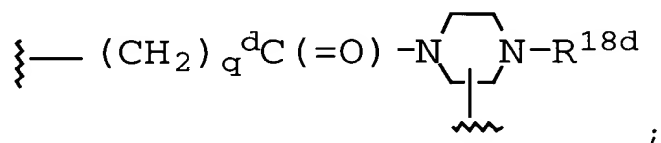
W<sup>d</sup> is selected from:

-(C(R<sup>12d</sup>)<sub>2</sub>)<sub>q</sub><sup>d</sup>C(=O)N(R<sup>13d</sup>)-, and

-C(=O)-N(R<sup>13d</sup>)-(C(R<sup>12d</sup>)<sub>2</sub>)<sub>q</sub><sup>d</sup>-;

10 X<sup>d</sup> is -C(R<sup>12d</sup>)(R<sup>14d</sup>)-C(R<sup>12d</sup>)(R<sup>15d</sup>)-; or

alternatively, W<sup>d</sup> and X<sup>d</sup> can be taken together to be



15 R<sup>12d</sup> is selected from H, halogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>4</sub>-C<sub>10</sub> cycloalkylalkyl, (C<sub>1</sub>-C<sub>4</sub> alkyl)carbonyl, aryl, and aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

R<sup>13d</sup> is selected from H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkylmethyl,  
20 and aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

R<sup>14d</sup> is selected from:

H, C<sub>1</sub>-C<sub>6</sub> alkylthio(C<sub>1</sub>-C<sub>6</sub> alkyl)-, aryl(C<sub>1</sub>-C<sub>10</sub> alkylthioalkyl)-, aryl(C<sub>1</sub>-C<sub>10</sub> alkoxyalkyl)-, C<sub>1</sub>-C<sub>10</sub> alkyl,  
25 C<sub>1</sub>-C<sub>10</sub> alkoxyalkyl, C<sub>1</sub>-C<sub>6</sub> hydroxyalkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>2</sub>-C<sub>10</sub> alkynyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>3</sub>-C<sub>10</sub> cycloalkylalkyl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, aryl, heteroaryl, CO<sub>2</sub>R<sup>17d</sup>, C(=O)R<sup>17d</sup>, and CONR<sup>17d</sup>R<sup>20d</sup>, provided that any of the above alkyl, cycloalkyl, aryl or

heteroaryl groups may be unsubstituted or substituted independently with 0-1 R<sup>16d</sup> or 0-2 R<sup>11d</sup>;

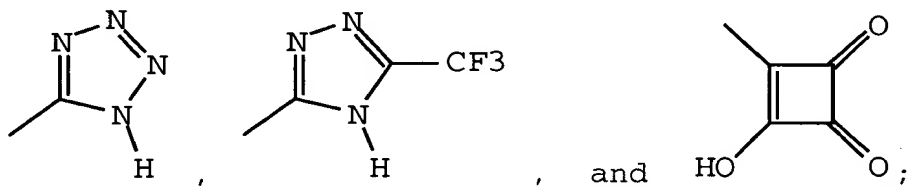
R<sup>15d</sup> is selected from:

- 5     H, R<sup>16d</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxyalkyl,  
C<sub>1</sub>-C<sub>10</sub> alkylaminoalkyl, C<sub>1</sub>-C<sub>10</sub> dialkylaminoalkyl, (C<sub>1</sub>-C<sub>10</sub>  
alkyl)carbonyl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)carbonyl, C<sub>1</sub>-C<sub>10</sub> alkenyl,  
C<sub>1</sub>-C<sub>10</sub> alkynyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>3</sub>-C<sub>10</sub> cycloalkylalkyl,  
aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, aryl,  
10     heteroaryl, CO<sub>2</sub>R<sup>17d</sup>, C(=O)R<sup>17d</sup>, CONR<sup>17d</sup>R<sup>20d</sup>, SO<sub>2</sub>R<sup>17d</sup>, and  
SO<sub>2</sub>NR<sup>17d</sup>R<sup>20d</sup>, provided that any of the above alkyl,  
cycloalkyl, aryl or heteroaryl groups may be  
unsubstituted or substituted independently with 0-2 R<sup>11d</sup>;

- 15     Y<sup>d</sup> is selected from:

-COR<sup>19d</sup>, -SO<sub>3</sub>H, -PO<sub>3</sub>H, tetrazolyl, -CONHNHSO<sub>2</sub>CF<sub>3</sub>, -  
CONHSO<sub>2</sub>R<sup>17d</sup>, -CONHSO<sub>2</sub>NHR<sup>17d</sup>, -NHCOCF<sub>3</sub>, -NHCONHSO<sub>2</sub>R<sup>17d</sup>, -  
NHSO<sub>2</sub>R<sup>17d</sup>, -OPO<sub>3</sub>H<sub>2</sub>, -OSO<sub>3</sub>H, -PO<sub>3</sub>H<sub>2</sub>, -SO<sub>3</sub>H, -SO<sub>2</sub>NHCOR<sup>17d</sup>, -  
SO<sub>2</sub>NHCO<sub>2</sub>R<sup>17d</sup>,

20     \_\_\_\_\_



R<sup>16d</sup> is selected from:

- 25     -N(R<sup>20d</sup>)-C(=O)-O-R<sup>17d</sup>,  
-N(R<sup>20d</sup>)-C(=O)-R<sup>17d</sup>,  
-N(R<sup>20d</sup>)-C(=O)-NH-R<sup>17d</sup>,  
-N(R<sup>20d</sup>)SO<sub>2</sub>-R<sup>17d</sup>, and  
-N(R<sup>20d</sup>)SO<sub>2</sub>-NR<sup>20d</sup>R<sup>17d</sup>;

R<sup>17d</sup> is selected from:

C<sub>1</sub>-C<sub>10</sub> alkyl optionally substituted with a bond to L<sub>n</sub>, C<sub>3</sub>-  
C<sub>11</sub> cycloalkyl optionally substituted with a bond to L<sub>n</sub>,  
aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- optionally substituted with a bond to  
 5 L<sub>n</sub>, (C<sub>1</sub>-C<sub>6</sub> alkyl)aryl optionally substituted with a bond  
to L<sub>n</sub>, heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- optionally substituted  
with a bond to L<sub>n</sub>, (C<sub>1</sub>-C<sub>6</sub> alkyl)heteroaryl optionally  
substituted with a bond to L<sub>n</sub>, biaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-  
optionally substituted with a bond to L<sub>n</sub>, heteroaryl  
 10 optionally substituted with a bond to L<sub>n</sub>, aryl optionally  
substituted with a bond to L<sub>n</sub>, biaryl optionally  
substituted with a bond to L<sub>n</sub>, and a bond to L<sub>n</sub>, wherein  
said aryl, biaryl or heteroaryl groups are also  
optionally substituted with 0-3 substituents selected  
 15 from the group consisting of: C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy,  
aryl, heteroaryl, halo, cyano, amino, CF<sub>3</sub>, and NO<sub>2</sub>;

R<sup>18d</sup> is selected from:

-H,  
 20 -C(=O)-O-R<sup>17d</sup>,  
-C(=O)-R<sup>17d</sup>,  
-C(=O)-NH-R<sup>17d</sup>,  
-SO<sub>2</sub>-R<sup>17d</sup>, and  
-SO<sub>2</sub>-NR<sup>20d</sup>R<sup>17d</sup>;

25

R<sup>19d</sup> is selected from: hydroxy, C<sub>1</sub>-C<sub>10</sub> alkyloxy,

C<sub>3</sub>-C<sub>11</sub> cycloalkyloxy, aryloxy, aryl(C<sub>1</sub>-C<sub>6</sub> alkoxy)-, C<sub>3</sub>-C<sub>10</sub>  
alkylcarbonyloxyalkyloxy, C<sub>3</sub>-C<sub>10</sub>  
alkoxycarbonyloxyalkyloxy, C<sub>2</sub>-C<sub>10</sub> alkoxycarbonylalkyloxy,  
 30 C<sub>5</sub>-C<sub>10</sub> cycloalkylcarbonyloxyalkyloxy,  
C<sub>5</sub>-C<sub>10</sub> cycloalkoxycarbonyloxyalkyloxy,  
C<sub>5</sub>-C<sub>10</sub> cycloalkoxycarbonylalkyloxy,

C<sub>7</sub>-C<sub>11</sub> aryloxy carbonylalkyloxy,  
C<sub>8</sub>-C<sub>12</sub> aryloxy carbonyloxyalkyloxy,  
C<sub>8</sub>-C<sub>12</sub> aryl carbonyloxyalkyloxy,  
C<sub>5</sub>-C<sub>10</sub> alkoxyalkyl carbonyloxyalkyloxy, C<sub>5</sub>-C<sub>10</sub> (5-alkyl-  
 5 1,3-dioxo-cyclopenten-2-one-yl)methyloxy, C<sub>10</sub>-C<sub>14</sub> (5-aryl-  
1,3-dioxo-cyclopenten-2-one-yl)methyloxy, and  
(R<sup>11d</sup>) (R<sup>12d</sup>)N-(C<sub>1</sub>-C<sub>10</sub> alkoxy)-;

10 R<sup>20d</sup> is selected from: H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>4</sub>-C<sub>11</sub>  
cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, and  
heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

R<sup>21d</sup> is selected from: COOH and NR<sup>6d</sup><sub>2</sub>;

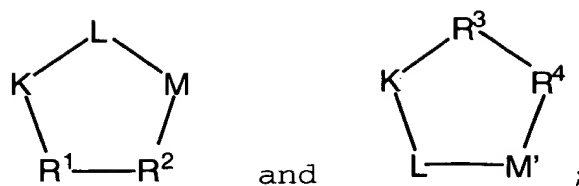
15 m<sup>d</sup> is 0-4;  
n<sup>d</sup> is 0-4;  
t<sup>d</sup> is 0-4;  
p<sup>d</sup> is 0-2;  
q<sup>d</sup> is 0-2; and  
r<sup>d</sup> is 0-2;

20

with the following provisos:

(1) t<sup>d</sup>, n<sup>d</sup>, m<sup>d</sup> and q<sup>d</sup> are chosen such that the number of atoms  
connecting R<sup>1d</sup> and Y<sup>d</sup> is in the range of 10-14; and  
 (2) n<sup>d</sup> and m<sup>d</sup> are chosen such that the value of n<sup>d</sup> plus m<sup>d</sup> is  
 25 greater than one unless U<sup>d</sup> is  
-(CH<sub>2</sub>)<sub>t</sub> Q<sup>d</sup> (CH<sub>2</sub>)<sub>m</sub> -;

or Q is a peptide selected from the group:



R<sup>1</sup> is L-valine, D-valine or L-lysine optionally substituted on the ε amino group with a bond to L<sub>n</sub>;

5

R<sup>2</sup> is L-phenylalanine, D-phenylalanine, D-1-naphthylalanine, 2-aminothiazole-4-acetic acid or tyrosine, the tyrosine optionally substituted on the hydroxy group with a bond to L<sub>n</sub>;

10

R<sup>3</sup> is D-valine;

R<sup>4</sup> is D-tyrosine substituted on the hydroxy group with a bond to L<sub>n</sub>;

15

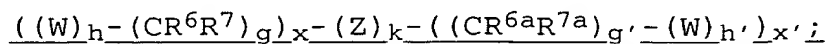
provided that one of R<sup>1</sup> and R<sup>2</sup> in each Q is substituted with a bond to L<sub>n</sub>, and further provided that when R<sup>2</sup> is 2-aminothiazole-4-acetic acid, K is N-methylarginine;

provided that at least one Q is a compound of Formula (Ia) or (Ib);

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

d' is 1-100;

L<sub>n</sub> is a linking group having the formula:



W is independently selected at each occurrence from the group:

O, S, NH, NHC(=O), C(=O)NH, NR<sup>8</sup>C(=O), C(=O)N R<sup>8</sup>, C(=O),  
C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO<sub>2</sub>, SO<sub>2</sub>NH,  
(OCH<sub>2</sub>CH<sub>2</sub>)<sub>s</sub>, (CH<sub>2</sub>CH<sub>2</sub>O)<sub>s'</sub>, (OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>)<sub>s''</sub>, (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>O)<sub>t</sub>, and  
 5 (aa)<sub>t'</sub>;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R<sup>10</sup>,  
 10 C<sub>3-10</sub> cycloalkyl substituted with 0-3 R<sup>10</sup>, and a 5-10  
membered heterocyclic ring system containing 1-4  
heteroatoms independently selected from N, S, and O and  
substituted with 0-3 R<sup>10</sup>;

15 R<sup>6</sup>, R<sup>6a</sup>, R<sup>7</sup>, R<sup>7a</sup>, and R<sup>8</sup> are independently selected at each  
occurrence from the group: H, =O, COOH, SO<sub>3</sub>H, PO<sub>3</sub>H, C<sub>1</sub>-C<sub>5</sub>  
alkyl substituted with 0-3 R<sup>10</sup>, aryl substituted with 0-3  
R<sup>10</sup>, benzyl substituted with 0-3 R<sup>10</sup>, and C<sub>1</sub>-C<sub>5</sub> alkoxy  
substituted with 0-3 R<sup>10</sup>, NHC(=O)R<sup>11</sup>, C(=O)NHR<sup>11</sup>,  
 20 NHC(=O)NHR<sup>11</sup>, NHR<sup>11</sup>, R<sup>11</sup>, and a bond to C<sub>H</sub>;

R<sup>10</sup> is independently selected at each occurrence from the  
group: a bond to C<sub>H</sub>, COOR<sup>11</sup>, C(=O)NHR<sup>11</sup>, NHC(=O)R<sup>11</sup>, OH,  
NHR<sup>11</sup>, SO<sub>3</sub>H, PO<sub>3</sub>H, -OPO<sub>3</sub>H<sub>2</sub>, -OSO<sub>3</sub>H, aryl substituted with  
 25 0-3 R<sup>11</sup>, C<sub>1-5</sub> alkyl substituted with 0-1 R<sup>12</sup>, C<sub>1-5</sub> alkoxy  
substituted with 0-1 R<sup>12</sup>, and a 5-10 membered  
heterocyclic ring system containing 1-4 heteroatoms  
independently selected from N, S, and O and substituted  
with 0-3 R<sup>11</sup>;

30 R<sup>11</sup> is independently selected at each occurrence from the  
group: H, alkyl substituted with 0-1 R<sup>12</sup>, aryl

substituted with 0-1  $R^{12}$ , a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1  $R^{12}$ ,  $C_{3-10}$  cycloalkyl substituted with 0-1  $R^{12}$ , polyalkylene glycol substituted with 0-1  $R^{12}$ , carbohydrate substituted with 0-1  $R^{12}$ , cyclodextrin substituted with 0-1  $R^{12}$ , amino acid substituted with 0-1  $R^{12}$ , polycarboxyalkyl substituted with 0-1  $R^{12}$ , polyazaalkyl substituted with 0-1  $R^{12}$ , and peptide substituted with 0-1  $R^{12}$ , wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to  $C_h$ ;

$R^{12}$  is a bond to  $C_h$ ;

15

$k$  is selected from 0, 1, and 2;

$h$  is selected from 0, 1, and 2;

$h'$  is selected from 0, 1, and 2;

$g$  is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

20 

$g'$  is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

$s$  is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

$s'$  is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

$s''$  is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

$t$  is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

25 

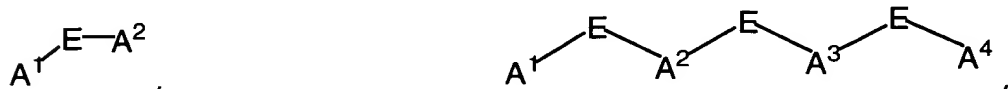
$t'$  is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

$x$  is selected from 0, 1, 2, 3, 4, and 5;

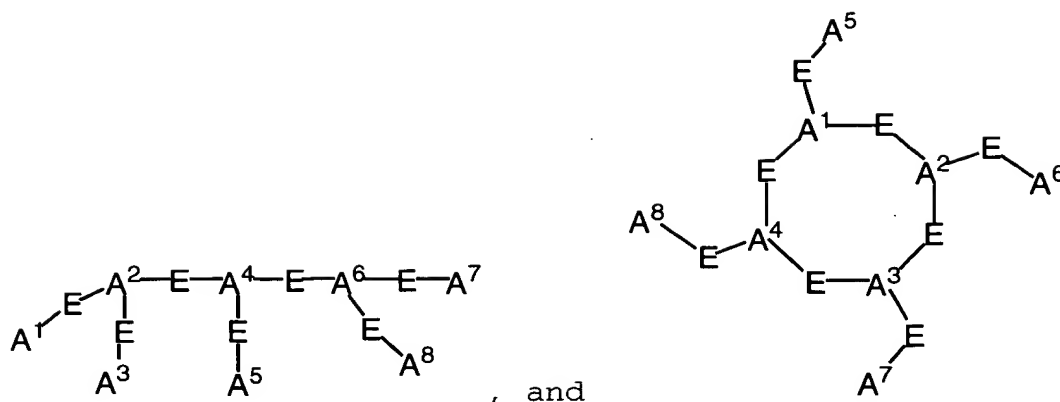
$x'$  is selected from 0, 1, 2, 3, 4, and 5;

30

$C_h$  is a metal bonding unit having a formula selected from the group:







$A^1, A^2, A^3, A^4, A^5, A^6, A^7,$  and  $A^8$  are independently selected at each occurrence from the group:  $NR^{13}, NR^{13}R^{14}, S, SH, S(Pg), O, OH, PR^{13}, PR^{13}R^{14}, P(O)R^{15}R^{16}$ , and a bond to  $L_n$ ;

$E$  is a bond, CH, or a spacer group independently selected at each occurrence from the group:  $C_1$ - $C_{10}$  alkyl substituted with 0-3  $R^{17}$ , aryl substituted with 0-3  $R^{17}$ ,  $C_{3-10}$  cycloalkyl substituted with 0-3  $R^{17}$ , heterocyclo- $C_{1-10}$  alkyl substituted with 0-3  $R^{17}$ , wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O,  $C_{6-10}$  aryl- $C_{1-10}$  alkyl substituted with 0-3  $R^{17}$ ,  $C_{1-10}$  alkyl- $C_{6-10}$  aryl- substituted with 0-3  $R^{17}$ , and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3  $R^{17}$ ;

$R^{13}$  and  $R^{14}$  are each independently selected from the group: a bond to  $L_n$ , hydrogen,  $C_1$ - $C_{10}$  alkyl substituted with 0-3  $R^{17}$ , aryl substituted with 0-3  $R^{17}$ ,  $C_{1-10}$  cycloalkyl substituted with 0-3  $R^{17}$ , heterocyclo- $C_{1-10}$  alkyl substituted with 0-3  $R^{17}$ , wherein the heterocyclo group

is a 5-10 membered heterocyclic ring system containing  
 1-4 heteroatoms independently selected from N, S, and O,  
C<sub>6-10</sub> aryl-C<sub>1-10</sub> alkyl substituted with 0-3 R<sup>17</sup>, C<sub>1-10</sub>  
alkyl-C<sub>6-10</sub> aryl- substituted with 0-3 R<sup>17</sup>, a 5-10  
 5 membered heterocyclic ring system containing 1-4  
 heteroatoms independently selected from N, S, and O and  
 substituted with 0-3 R<sup>17</sup>, and an electron, provided that  
 when one of R<sup>13</sup> or R<sup>14</sup> is an electron, then the other is  
 also an electron;

10

alternatively, R<sup>13</sup> and R<sup>14</sup> combine to form =C(R<sup>20</sup>)(R<sup>21</sup>);

15

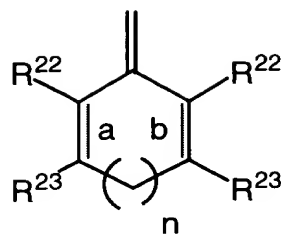
R<sup>15</sup> and R<sup>16</sup> are each independently selected from the group: a  
 bond to L<sub>n</sub>, -OH, C<sub>1-C10</sub> alkyl substituted with 0-3 R<sup>17</sup>,  
C<sub>1-C10</sub> alkyl substituted with 0-3 R<sup>17</sup>, aryl substituted  
 with 0-3 R<sup>17</sup>, C<sub>3-10</sub> cycloalkyl substituted with 0-3 R<sup>17</sup>,  
 heterocyclo-C<sub>1-10</sub> alkyl substituted with 0-3 R<sup>17</sup>, wherein  
 the heterocyclo group is a 5-10 membered heterocyclic  
 ring system containing 1-4 heteroatoms independently  
 20 selected from N, S, and O, C<sub>6-10</sub> aryl-C<sub>1-10</sub> alkyl  
substituted with 0-3 R<sup>17</sup>, C<sub>1-10</sub> alkyl-C<sub>6-10</sub> aryl-  
substituted with 0-3 R<sup>17</sup>, and a 5-10 membered  
 heterocyclic ring system containing 1-4 heteroatoms  
 independently selected from N, S, and O and substituted  
 25 with 0-3 R<sup>17</sup>;

25

30

R<sup>17</sup> is independently selected at each occurrence from the  
 group: a bond to L<sub>n</sub>, =O, F, Cl, Br, I, -CF<sub>3</sub>, -CN,  
 -CO<sub>2</sub>R<sup>18</sup>, -C(=O)R<sup>18</sup>, -C(=O)N(R<sup>18</sup>)<sub>2</sub>, -CHO, -CH<sub>2</sub>OR<sup>18</sup>,  
 -OC(=O)R<sup>18</sup>, -OC(=O)OR<sup>18a</sup>, -OR<sup>18</sup>, -OC(=O)N(R<sup>18</sup>)<sub>2</sub>,  
 -NR<sup>19</sup>C(=O)R<sup>18</sup>, -NR<sup>19</sup>C(=O)OR<sup>18a</sup>, -NR<sup>19</sup>C(=O)N(R<sup>18</sup>)<sub>2</sub>,

- NR<sup>19</sup>SO<sub>2</sub>N(R<sup>18</sup>)<sub>2</sub>, -NR<sup>19</sup>SO<sub>2</sub>R<sup>18a</sup>, -SO<sub>3</sub>H, -SO<sub>2</sub>R<sup>18a</sup>, -SR<sup>18</sup>,  
-S(=O)R<sup>18a</sup>, -SO<sub>2</sub>N(R<sup>18</sup>)<sub>2</sub>, -N(R<sup>18</sup>)<sub>2</sub>, -NHC(=S)NHR<sup>18</sup>, =NOR<sup>18</sup>,  
NO<sub>2</sub>, -C(=O)NHR<sup>18</sup>, -C(=O)NHN(R<sup>18</sup>)R<sup>18a</sup>, -OCH<sub>2</sub>CO<sub>2</sub>H,  
 5 2-(1-morpholino)ethoxy, C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>2</sub>-C<sub>4</sub> alkenyl, C<sub>3</sub>-C<sub>6</sub>  
cycloalkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylmethyl, C<sub>2</sub>-C<sub>6</sub> alkoxyalkyl,  
aryl substituted with 0-2 R<sup>18</sup>, and a 5-10 membered  
heterocyclic ring system containing 1-4 heteroatoms  
independently selected from N, S, and O;
- 10 R<sup>18</sup>, R<sup>18a</sup>, and R<sup>19</sup> are independently selected at each  
occurrence from the group: a bond to L<sub>n</sub>, H, C<sub>1</sub>-C<sub>6</sub> alkyl,  
phenyl, benzyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, halide, nitro, cyano, and  
trifluoromethyl;
- 15 Pg is a thiol protecting group;
- R<sup>20</sup> and R<sup>21</sup> are independently selected from the group: H,  
C<sub>1</sub>-C<sub>10</sub> alkyl, -CN, -CO<sub>2</sub>R<sup>25</sup>, -C(=O)R<sup>25</sup>, -C(=O)N(R<sup>25</sup>)<sub>2</sub>,  
C<sub>2</sub>-C<sub>10</sub> 1-alkene substituted with 0-3 R<sup>23</sup>, C<sub>2</sub>-C<sub>10</sub> 1-alkyne  
 20 substituted with 0-3 R<sup>23</sup>, aryl substituted with 0-3 R<sup>23</sup>,  
unsaturated 5-10 membered heterocyclic ring system  
containing 1-4 heteroatoms independently selected from N,  
S, and O and substituted with 0-3 R<sup>23</sup>, and unsaturated  
C<sub>3</sub>-C<sub>10</sub> carbocycle substituted with 0-3 R<sup>23</sup>;
- 25 alternatively, R<sup>20</sup> and R<sup>21</sup>, taken together with the divalent  
carbon radical to which they are attached form:



$R^{22}$  and  $R^{23}$  are independently selected from the group: H,  $R^{24}$ ,  $C_1$ - $C_{10}$  alkyl substituted with 0-3  $R^{24}$ ,  $C_2$ - $C_{10}$  alkenyl substituted with 0-3  $R^{24}$ ,  $C_2$ - $C_{10}$  alkynyl substituted with 0-3  $R^{24}$ , aryl substituted with 0-3  $R^{24}$ , a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3  $R^{24}$ , and  $C_{3-10}$  carbocycle substituted with 0-3  $R^{24}$ ;

alternatively,  $R^{22}$ ,  $R^{23}$  taken together form a fused aromatic or a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

**a** and **b** indicate the positions of optional double bonds and **n** is 0 or 1;

$R^{24}$  is independently selected at each occurrence from the group: =O, F, Cl, Br, I,  $-CF_3$ ,  $-CN$ ,  $-CO_2R^{25}$ ,  $-C(=O)R^{25}$ ,  $-C(=O)N(R^{25})_2$ ,  $-N(R^{25})_3^+$ ,  $-CH_2OR^{25}$ ,  $-OC(=O)R^{25}$ ,  $-OC(=O)OR^{25a}$ ,  $-OR^{25}$ ,  $-OC(=O)N(R^{25})_2$ ,  $-NR^{26}C(=O)R^{25}$ ,  $-NR^{26}C(=O)OR^{25a}$ ,  $-NR^{26}C(=O)N(R^{25})_2$ ,  $-NR^{26}SO_2N(R^{25})_2$ ,  $-NR^{26}SO_2R^{25a}$ ,  $-SO_3H$ ,  $-SO_2R^{25a}$ ,  $-SR^{25}$ ,  $-S(=O)R^{25a}$ ,  $-SO_2N(R^{25})_2$ ,  $-N(R^{25})_2$ ,  $=NOR^{25}$ ,  $-C(=O)NHOR^{25}$ ,  $-OCH_2CO_2H$ , and 2-(1-morpholino)ethoxy; and,

R<sup>25</sup>, R<sup>25a</sup>, and R<sup>26</sup> are each independently selected at each occurrence from the group: hydrogen and C<sub>1</sub>-C<sub>6</sub> alkyl.

65. (Amended) A therapeutic metallopharmaceutical radiopharmaceutical composition comprising at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof, and a radiopharmaceutical comprising:

a) a therapeutic metal; and

b) a compound;

wherein the compound comprises:

i) a chelator capable of chelating the therapeutic metal;

ii) a targeting moiety; and

iii) 0-1 linking groups between the targeting moiety and chelator; or

a pharmaceutically acceptable salt thereof,

wherein the targeting moiety is an indazole nonpeptide that binds to a receptor that is upregulated during angiogenesis.

~~according to claim 11, wherein the metallopharmaceutical is a therapeutic radiopharmaceutical, further comprising at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof.~~

66. (Amended) A therapeutic radiometallopharmaceutical composition according to claim 65, wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide, elliptinium acetate, ketanserin, doxifluridine, etretinate, isotretinoin, streptozocin,

nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitio stanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftotox, interleukin-2, and leutinizing hormone releasing factor.

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67. (Amended) A therapeutic radiometallopharmaceutical composition according to claim 65, wherein radiosensitizer agent is selected from the group consisting of 2-(3-nitro-1,2,4-triazol-1-yl)-N-(2-methoxyethyl)acetamide, N-(3-nitro-4-quinolinyl)-4-morpholinecarboxamidine, 3-amino-1,2,4-benzotriazine-1,4-dioxide, N-(2-hydroxyethyl)-2-nitroimidazole-1-acetamide, 1-(2-nitroimidazol-1-yl)-3-(1-piperidinyl)-2-propanol, and 1-(2-nitro-1-imidazolyl)-3-(1-aziridino)-2-propanol.

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68. (Amended) A method of treating cancer in a patient comprising: administering to a patient in need thereof a therapeutic radiopharmaceutical and at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof wherein the therapeutic radiopharmaceutical comprises:

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a) a therapeutic metal; and

b) a compound;

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wherein the compound comprises:

- i) a chelator capable of chelating the therapeutic metal;
- ii) a targeting moiety; and
- iii) 0-1 linking groups between the targeting moiety and chelator; or

a pharmaceutically acceptable salt thereof;  
wherein the targeting moiety is an indazole non-peptide that  
binds to a receptor that is upregulated during angiogenesis.  
~~Claim 19 or a pharmaceutically acceptable salt thereof, and at~~  
5 ~~least one agent selected from the group consisting of a~~  
~~chemotherapeutic agent and a radiosensitizer agent, or a~~  
~~pharmaceutically acceptable salt thereof.~~